

WE CLAIM:

1. A method for detection of metastatic potential comprising detecting expression of flt-4 in a prostate cell, wherein expression of flt-4 indicates that said cell has metastatic potential.
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2. A method for detection of metastatic potential comprising identifying a prostate cell in a body fluid sample obtained from a subject and detecting expression of flt-4 in said cell, wherein expression of flt-4 indicates that said cell is a prostate cancer cell that has
10 metastatic potential or is a secondary prostate tumor metastasis, or is derived therefrom.
3. The method according to claim 1 or 2 in which the prostate cell is identified by using an antibody or a portion thereof that binds to a prostate cell-specific marker.
- 15 4. The method according to claim 3 in which the prostate cell-specific marker is selected from the group consisting of prostate-specific antigen (PSA), prostate-specific membrane antigen (PSMA), prostate secretory protein (PSP), prostate acid phosphatase (PAP), human glandular kallekrein 2 (HK-2), prostate stem cell antigen (PSCA) and PTI-1.
- 20 5. The method according to claim 1 or 2 in which flt-4 expression is detected using an antibody or a portion thereof that binds to flt-4.
6. The method according to claim 1 or 2 in which flt-4 expression is detected using a nucleic acid molecule, said molecule comprising a nucleotide sequence consisting of a
25 sequence of at least 6 contiguous nucleotides complementary to the nucleotide sequence set forth in SEQ ID NO:1.
7. The method according to claim 2 in which the body fluid is blood, urine or semen.
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8. The method according to claim 2 in which identifying the prostate cell and detecting flt-4 expression are performed simultaneously.
9. The method according to claim 8 in which any immunofluorescence assay is
35 employed.

10. The method according to claim 9 in which the immunofluorescence assay employs a flow cytometer or a laser scanning cytometer.

11. A method for diagnosing metastatic prostate cancer in a subject comprising
5 identifying a prostate cell in a body fluid sample obtained from the subject and detecting expression of flt-4 in the prostate cell, wherein expression of flt-4 in a prostate cell indicates that the subject has metastatic prostate cancer.

12. A method for determining the prognosis of a subject with prostate cancer
10 comprising identifying a prostate cell in a body fluid sample obtained from a subject with prostate cancer and detecting expression of flt-4 in the prostate cell, wherein expression of flt-4 in said cell indicates that the subject has a worse prognosis as compared to a second subject in whose prostate cell no flt-4 expression or activity is detected.

13. A method of treating, inhibiting or preventing a secondary prostate tumor metastasis comprising administering to a subject in which such treatment, inhibition or prevention is desired a therapeutically effective amount of a molecule that inhibits flt-4 expression or activity.

14. The method according to claim 13 in which the molecule is a protein
20 comprising a fragment of flt-4, which fragment consists of at least the amino acid sequence set forth in SEQ ID NO:2, which protein acts as a competitive inhibitor of flt-4 binding to its ligand VEGF-C.

15. The method according to claim 14 in which the protein is soluble.

16. The method according to claim 13 in which the molecule is a nucleic acid molecule comprising a nucleotide sequence which encodes for a fragment of flt-4, which fragment acts as a competitive inhibitor of flt-4 binding to its ligand VEGF-C.

17. The method according to claim 13 in which the molecule is an antisense oligonucleotide comprising a nucleotide sequence consisting of at least 6 contiguous nucleotides complementary to the nucleotide sequence set forth in SEQ ID NO:1.

18. The method according to claim 17 in which the antisense oligonucleotide
35 comprises the nucleotide sequence 5'-GGCGCCCCGCTGCAT-3' (SEQ ID NO:3).

19. The method according to claim 13 in which the molecule is an antibody or a portion thereof that binds to flt-4.

20. A method for screening for a molecule that treats, inhibits or prevents a
5 secondary prostate tumor metastasis comprising contacting a prostate cell that expresses flt-4 with a candidate molecule and comparing the level of flt-4 expression in the cell so contacted with a prostate cell expressing flt-4 not so contacted, wherein a lower level of flt-4 expression in the contacted cell as compared to the non-contacted cell indicates that the candidate molecule has activity in treating, inhibiting or preventing secondary prostate
10 tumor metastases.

21. A method for screening for a molecule that treats, inhibits or prevents a secondary prostate tumor metastasis comprising measuring the levels of complex formed from flt-4 and VEGF-C in the presence of a candidate molecule under conditions conducive
15 to the formation of said complex; and comparing levels of said complex that are formed in the absence of the molecule, wherein a lower level of said complex in the presence of the molecule indicates that the candidate molecule has activity in treating, inhibiting or preventing secondary prostate tumor metastases.

20 22. A method for screening for a molecule that treats, inhibits or prevents a secondary prostate tumor metastasis comprising measuring the levels of complex formed from flt-4 and VEGF-D in the presence of a candidate molecule under conditions conducive to the formation of said complex; and comparing levels of said complex that are formed in the absence of the molecule, wherein a lower level of said complex in the presence of the
25 molecule indicates that the candidate molecule has activity in treating, inhibiting or preventing secondary prostate tumor metastases.

23. A method of monitoring the efficacy of a method of treatment or inhibition of metastatic prostate cancer comprising measuring the level of expression or activity of flt-4
30 in prostate cells obtained from a subject wherein said sample is taken from said subject after the application of said method and compared to (a) said level in a sample taken from said subject prior to the application of said method or (b) a standard level associated with the pretreatment stage of metastatic prostate cancer, in which a decrease in the level of flt-4 expression or activity in said sample taken after application of said method relative to the
35 level of flt-4 expression or activity in said sample taken before application of said method or to said standard level indicates that said method is effective.

24. A pharmaceutical composition comprising a protein, which protein comprises a fragment of flt-4, which fragment consists of at least the amino acid sequence set forth in SEQ ID NO:2, which protein acts as a competitive inhibitor of flt-4 binding to its ligand VEGF-C; and a pharmaceutically acceptable carrier.

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25. The composition according to claim 24 in which the protein is soluble.

26. A pharmaceutical composition comprising a nucleic acid, which nucleic acid comprises a nucleotide sequence which encodes for a fragment of flt-4, which fragment acts
10 as a competitive inhibitor of flt-4 binding to its ligand VEGF-C; and a pharmaceutically acceptable carrier.

27. A pharmaceutical composition comprising an antisense oligonucleotide, which oligonucleotide comprises a nucleotide sequence consisting of at least 6 contiguous
15 nucleotides complementary to the nucleotide sequence set forth in SEQ ID NO:1; and a pharmaceutically acceptable carrier.

28. The composition according to claim 27 in which the antisense oligonucleotide comprises the nucleotide sequence 5'-GGCGCCCCGCTGCAT-3' (SEQ ID NO:3).
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29. A pharmaceutical composition comprising an antibody or a portion thereof that binds to flt-4; and a pharmaceutically acceptable carrier.

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